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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/895,913	06/29/2001	Harold Kleanthous	06132/043002	3260

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EXAMINER
PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
1645	11

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/881,752	Kleanthous et al
Examiner	**Art Unit**
Portner	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 4, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) ~~1-39~~ 1-38 is/are pending in the application.

4a) Of the above, claim(s) 8-29, 38 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-5 and 30-35* is/are rejected.

7) ☒ Claim(s) *6, 7, and 37* is/are objected to.

8) ☒ Claims ~~1-39~~ 1-38 are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-38 are pending.

Information Disclosure Statement

1. The information disclosure statement filed October 17, 2001 has been considered.

Election/Restriction

2. Claims 8-29 and 38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups II-V and non-elected inventions in Group I, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 10.

3. Applicant's election without traverse of Group I, claims 1-7 and 30-37, specifically the isolated nucleic acid molecule of SEQ ID NO 120, vectors, host cells, and a method of using said host cells to produce a polypeptide, classified in class 536, subclass in Paper No. 10 is acknowledged. The restriction/election requirement made of record on paper number 8, is deemed to be proper and therefore made Final.

Specification

4. Claims 6-7 and 37 are objected to under 37 CFR 1.75© as being in improper form because a multiple dependent claim must refer to preceding claims in the alternative. See MPEP § 608.01(n). One or more claims may be presented in dependent form, referring back to and

further limiting another claim or claims in the same application. Any dependent claim which refers to more than one other claim ("multiple dependent claim") shall refer to such other claims in the alternative only. A multiple dependent claim may refer in the alternative to only one set of claims. Section 112 allows reference to only a particular claim.. Correction is requested.

Claim Rejections - 35 U.S.C. § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-5 and 30-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the full scope of the claimed invention.

This is a written description rejection over homologous polynucleotides that encode a polypeptide the comprises an amino acid sequence that is a homolog to a sequence contained in SEQ ID NO:20 or is a homolog of SEQ ID NO:20.

VSP 2/03

The claims are drawn to isolated polynucleotides that encode polypeptides of any size that comprise an amino acid sequence that is homologous to the amino acid sequence defined by SEQ ID NO 120. The claims, as written, are being read as representative of a genus of genes that encode polypeptides and a genus of polynucleotides that encode for a polypeptide that shares an amino acid sequence with SEQ ID NO 120; the claimed invention not being limited to a polynucleotide encoding Helicobacter polypeptides but may encode a homolog of an amino acid sequence of a Helicobacter polypeptide as the claims recite "comprising" open language.

The only coding sequence for a full length protein elected is SEQ ID NO 120. No other full length coding sequences for a homolog of SEQ ID NO 120 is described. No allelic variants are described. No polynucleotide sequences are disclosed that have had insertions, deletions, or substitutions into any region of SEQ ID NO 120. No genes that only share 10, 20, 50, 75 or 100 amino acids of a polypeptide homolog of SEQ ID No 120 (387 amino acids) are described.

A nucleic acid sequence which codes for a polypeptide which is within the scope of the claims could differ from that which has been disclosed, this corresponds to hundreds of variations in the nucleic acid sequences being claimed. The specific codons or nucleotides which differ from the polynucleotide that encodes SEQ ID NO 120, could encode a polypeptide with amino acid deletions, substitutions or insertions. No specific locations for the deletions, substitutions or insertions are disclosed therefore the number nucleotides that encodes the recited polypeptide and sequence of nucleic acids coding for polypeptides which are encompassed by proteinaceous material which is homologous to SEQ ID NO 120 can not be readily be ascertained.

A representative number of species defined by structure and function for the genus of genes now claimed polynucleotides has not been described. Only a nucleotide sequence that encodes SEQ ID NO 120 (amino acid sequence) has been disclosed. No vectors have been described that comprise variant genes of the disclosed coding region of SEQ ID NO 120 and encode homologous polypeptides or homologous Helicobacter polypeptides.

Claim 4 is drawn to isolated polynucleotides that are DNA molecules that are amplifyable or can be cloned by polymerase chain reaction from any Helicobacter genome. While sequences could be identified that would hybridize to SEQ ID NO 120, what characteristics would be required to determine the identified nucleic acid encodes a Helicobacter polypeptide or antigenic fragment has not been described, nor have the homologous polynucleotides been defined as encoding a polypeptide of any specific function. How one would know, that the identified polynucleotide encodes a polypeptide of the instant invention has not been described. What polynucleotide sequences would be specifically Helicobacter polynucleotide sequences, differentiated from any other nucleic acid sequence has not been disclosed.

The sequences that are amplifyable or cloned by polymerase chain reaction need not be directed to the full length sequences that encode SEQ ID NO 120 (nucleotide sequence), but may be directed to any portion that encodes a polypeptide the is a homolog of the elected SEQ ID NO 120. No populations of antibodies, that are known to be Helicobacter specific and SEQ ID NO 120 specific, have been disclosed to define the encoded polypeptide as being representative of the claimed genus. While antibodies can be used to identify a polypeptide or antigenic fragment, the

structure and function of the polypeptide or antigenic fragment is not defined by any antibody binding thereto, nor does it show that Applicant had possession of the variant polynucleotides that encode polypeptides at the time of filing.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only an isolated polynucleotide consisting of a nucleotide sequence encoding SEQ ID NO:120, but not the full breadth of the claim meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Example 7, found on the USPTO website.

8. Claims 1-5,30-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

All claims under examination recite non-elected inventions and therefore do not distinctly claim Applicant's elected invention.

Claim 1 recite an improper Markush group as the recited sequences have not been shown to share a common structure and function.

Claim 35 recites the phrase "is unable to replicate and to substantially integrate in a mammalian genome"; it is not clear what the meaning of the phrase means as the word "substantially" is a relative term and therefore does not particularly point out and distinctly claim the subject matter which applicant regards as the invention. If the plasmid is unable to replicate and the DNA does not integrate into the mammalian genome, it is not clear how t he claimed the DNA molecule would be "placed under conditions for expression in a mammalian cell. What are the conditions; sterile water ?

Claim Rejections - 35 U.S.C. § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Taylor et al (1990) and polynucleotide accession number U27271, July 1995).

(Claim 1) Taylor et al disclose an isolated polynucleotide that encodes an amino acids sequence of SEQ ID No 120, wherein the polynucleotide encodes a homolog amino acid sequence of SEQ ID No 120 which was obtained from Campylobacter jejuni (see amino acid sequence alignment provide with SEQ ID No 120, which the EMBL polynucleotide sequence encodes, the publicly available date for the polynucleotide being "created date" July 4, 1995).

(Claim 2) The isolated polynucleotide accession number U27271, encoded the major form of the polypeptide relative to a mature form of a Helicobacter polypeptide,

(Claim 3) wherein the polynucleotide was a DNA molecule.

(Claims 4-5) The homolog amino acid sequence encoded by the Campylobacter jejuni polynucleotide (encodes consensus amino acid sequence of an HtrA protein, which is "GNSGGAL" as evidenced by Loosemore et al, (US Pat. 6,153,580) col. 14, Example 4, consensus sequences SEQ ID No 17), could be amplified by polymerase chain reaction from a Helicobacter pylori genome, in light of the fact that SEQ ID No 120 at amino acid positions 131-136, sets forth the consensus sequence encoded by the polynucleotide of Campylobacter jejuni.

The reference anticipates the instantly claimed invention as now claimed.

11. Claims 1-5, 32, 34, 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Bukanov et al (1994) as evidenced by Klenthous, H; Clayton, C.L et al (1994) and Tomb et al (1997).

Bukanov et al disclose a composition that comprises an isolated Helicobacter pylori polynucleotide designated "htrA" which encodes a heat shock protein, wherein the polynucleotide was cloned into miniset clone numbers 15,16, and 17, and was also identified in 34 clones containing NotI fragment B (see page 515, Table shown at top of page) based upon the utilization of PCR amplification (see page 516, Table 2) , primer numbers 38-39.

The compositions of Bukanov et al that comprised a polynucleotide that encodes for a heat shock protein, HtrA, based upon a gene determined to be an htrA gene, and were cloned first into a Lorist6 vector, and then into Lambda phage particles (see page 520, col. 1, paragraph 3) and then transduced into E.coli strain DH5-alpha (see page 520, col. 2, first and second paragraphs). The clones were combined with LB broth, a type of pharmaceutically acceptable carrier. Bukanov et al utilized a deposited strain of Helicobacter pylori, NTC11638, for the isolation and cloning of the htrA gene. Methods of making, and specific guidance for obtaining the htrA gene are disclosed. Clearly the Bukanov et al reference is enabled for the isolated htrA gene of Helicobacter pylori, NCTC11638, as well as is enabled for vectors and host cells that comprise the isolated polynucleotide which would be a homolog of SEQ ID NO 120 as it was obtained in the instant Application from a different strain of Helicobacter pylori.

As the instantly claimed invention is not limited to the polynucleotide that encodes SEQ ID NO 120, or any specific amino acid sequence that is a homolog of an amino acid sequence of SEQ ID NO 120 , the isolated Helicobacter pylori htrA polynucleotide of Bukanov (NotI fragment B), vectors and host cell (miniset, cosmid and E.coli clones comprising the polynucleotide) compositions would inherently comprise a homolog amino acid sequence of SEQ ID No 120, as Tomb et al provides evidence that SEQ ID No 120, is encoded by an Helicobacter pylori htrA gene, which encodes an Helicobacter pylori HtrA protein (100% sequence identity with SEQ ID NO 120) which is same or equivalent H.pylori gene of Bukanov et al.

Kleanthous, H and Clayton, C et al (1994, abstract title; Clayton, C was cited to provide information for primers in Bukanov et al, bottom of page 516, primers 38 and 39) also provide evidence that Helicobacter pylori produces an htrA gene that encodes an HtrA heat shock protein, which is further supported by evidence provided by Tomb et al discussed above.

Bukanov et al inherently anticipates the instantly claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. "The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art".

12. Claims 1-5, 32, 34, 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Kleanthous et al (1991/1994).

Kleanthous et al disclose the molecular cloning of Helicobacter pylori htrA gene (see title and entire document). The isolated polynucleotide was amplified by polymerase chain reaction (see page 199, Figure 3, and paragraph 2), as well as cloned into a viral vector (lambda phage, see page 196, paragraph 2) into E.coli (host cell, see page 197, paragraph 2) and expressed as a polypeptide (see Figures 1-2,page 197). The polynucleotide sequence encoded an amino acid sequence shown in Figure 2, which comprises an amino acid sequence of SEQ ID NO 120. Inherently the reference anticipates the instantly claimed invention.

Allowable Subject Matter

13. Claims limited to SEQ ID NO 120, would define allowable subject matter.

Conclusion

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

15. Dougan et al (WO91/15572) is cited to show in Figure 1, an isolated polynucleotide molecule that is a homolog of the instantly claimed invention directed to/* SEQ ID No 120.

16. Krivan et al (US Pat. 5,679,547) is cited to show SEQ ID No 1, Figures 7A-7D, an isolated polynucleotide molecule that is a homolog of the instantly claimed invention directed to SEQ ID No 120.

17. Loosmore et al (US Pat. 6,153,580 or WO96/03506(Figure 2)) is cited to show Haemophilus influenza protease nucleic acid and amino acid sequences (see figure 2 and col. 14, Example 4, consensus sequences SEQ ID NO 18 and SEQ ID No 17).

18. Miller et al (US Pat. 5,830,740) is cited to show a serine protease of Pyrobaculum aerophilum, and discloses both the nucleic acid and the amino acid sequence that encode the serine protease.

19. Polynucleotide homologs of the instantly claimed SEQ ID NO 120, that encode an amino acid of SEQ ID NO 120 include:

a. EMBL Accession Numbers:

i. U07351, Brucella abortus HtrA antigen (1995);
ii. X82628, Campylobacter jejuni htrA gene (submitted in 1994 and 1995)
iii. M3119.1, Chlamydia trachomatis antigen (1990);
iv. M36536, E.coli HtrA gene (1990);
v. U15180, Mycobacterium leprae (May 1995);
vi. L20127, Rochalimaea henselae HtrA antigen (1993);
vii. X54548, Salmonella typhimurium heat shock protein (1992);
viii. D90905, Synechocystis (October 1996); and
ix. X94153, Yersinia enterocolitica htrA gene (December 1995).

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
February 13, 2003

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